Claims

1. A method for detecting the presence of a IgG4 polypeptide having a selected disulfide linkage pattern in a sample comprising,

loading a sample containing a polypeptide having a selected disulfide linkage pattern, wherein the sample comprises an inhibitor of disulfide bond rearrangement, onto a chip comprising a channel having a separation medium effective to act as an obstacle to the migration of the polypeptide having a selected disulfide linkage pattern, and at least two electrodes disposed within the channel to induce an electric field,

applying an electric field across the separation medium of the chip whereby a separation of the IgG4 polypeptide having a selected disulfide linkage pattern as compared to a IgG4 polypeptide not having the selected disulfide linkage pattern is achieved, and

determining the presence of the IgG4 polypeptide having a selected disulfide linkage pattern.

2. A method for detecting the presence of a polypeptide having a selected disulfide linkage pattern in a sample consisting of a mixture of polypeptide multimers having two or more polypeptide chains and comprising at least one disulfide linkage between the polypeptide chains comprising,

loading a sample containing the mixture of polypeptide multimers, wherein the sample comprises an inhibitor of disulfide bond rearrangement, onto a chip comprising a channel having a separation medium effective to act as an obstacle to the migration of the polypeptide having a selected disulfide linkage pattern, and at least two electrodes disposed within the channel to induce an electric field,

applying an electric field across the separation medium of the chip whereby a separation of the polypeptide having a selected disulfide linkage pattern as compared to a polypeptide not having the selected disulfide linkage pattern is achieved, and determining the presence of the polypeptide having a selected disulfide linkage pattern.

3. The method of claim 1 or 2, wherein the inhibitor is a sulfhydryl alkylating reagent.

4. The method of claim 3, wherein the sulfhydryl alkylating reagent is selected from the group consisting of iodoacetamide and N-ethylmaleimide (NEM).

5. The method of claim 4, wherein the sulfhydryl alkylating reagent is N-ethylmaleimide (NEM).

6. The method of claim 5, wherein the amount of N-ethylmaleimide (NEM) is between about 1mM to about 10 mM.

7. The method of claim 1 or 2, wherein the method further comprises determining the presence of a polypeptide impurity.

8. The method of claim 1, wherein the IgG4 polypeptide having a selected disulfide linkage pattern is a half-antibody.

9. The method of claim 2, wherein the polypeptide having a selected disulfide linkage is a half-antibody.

10. The method of claim 9, wherein the half-antibody is of the IgG4 class.

11. The method of claim 1, wherein the IgG4 polypeptide having a selected disulfide linkage pattern is recombinantly produced.

12. The method of claim 1 or 2, wherein the polypeptide is recombinantly produced.

13. The method of claim 1 or 2, wherein the polypeptide having a selected disulfide linkage pattern is recombinantly produced.

14. The method of claim 1, wherein, the IgG4 polypeptide not having the selected disulfide linkage pattern is an anti-integrin antibody.

15. The method of claim 2, wherein the mixture comprises an anti-integrin antibody.

16. The method of claim 14 or 15, wherein the anti-integrin antibody is recombinantly produced.

17. The method of claim 1 or 2, wherein the sample is obtained from the growth medium of a cell culture.

18. The method of claim 1 or 2, wherein the sample comprises about 1 to about 5000 ug/ml of a polypeptide having a selected disulfide linkage pattern.

19. The method of claim 1 or 2, wherein the separation medium is a gel polymer.

20. The method of claim 1 or 2, wherein the separation medium is non-reducing.

21. The method of claim 1 or 2, wherein the migration of the polypeptide is detected using a fluorescence detector.

22. The method of claim 1 or 2, wherein the electric field is non-alternating.

23. The method of claim 1 or 2, wherein the separation further comprises isoelectric focusing.

24. The method of claim 1 or 2, wherein the separation is according to the molecular weight of the polypeptide.

25. The method of claim 1 or 2, wherein the chip comprises a precast gel polymer.

26. A kit for detecting the presence of a polypeptide having a selected disulfide linkage pattern comprising, a chip and instructions for carrying out the method of claim 1.

27. A kit for determining the purity of a therapeutic polypeptide having a selected disulfide linkage pattern comprising, a chip and instructions for carrying out the method of claim 1.

28. The kit of claim 26 or 27, wherein the kit further comprises a component selected from the group consisting of, separation medium, non-reducing buffer, protein dye, formulation buffer, and means for inducing an electric field through a separation medium.

29. The kit of claim 26 or 27, wherein the kit further comprises instructions for determining the presence of a polypeptide impurity.

30. The kit of claim 26 or 27, wherein the kit further comprises one or more polypeptide standards.

31. A method of inhibiting disulfide bond rearrangement, wherein the polypeptide is incubated with a sulfhydryl alkylating agent selected from the group consisting of iodoacetamide and N-ethylmaleimide (NEM).

32. The method of claim 31, wherein the sulfhydryl alkylating reagent is N-ethylmaleimide (NEM).

33. The method of claim 32, wherein the concentration of N-ethylmaleimide (NEM) is between about 1 mM to about 10 mM.

34. The method of claim 31, wherein the disulfide bond rearrangement occurs upon exposure to heat.

35. A composition comprising a polypeptide and inhibitor of disulfide bond rearrangement, wherein the inhibitor is a sulfhydryl alkylating agent.

36. The composition of claim 35, wherein the sulfhydryl alkylating agent is selected from the group consisting of iodoacetamide and N-ethylmaleimide (NEM).

37. The composition of claim 36, wherein the sulfhydryl alkylating reagent is N-ethylmaleimide (NEM).

38. The composition of claim 37, wherein the concentration of N-ethylmaleimide (NEM) is between about 1 to about 10 mM.

39. The composition of claim 35, wherein the polypeptide is a multimeric polypeptide.

40. The composition of claim 39, wherein multimeric polypeptide is an antibody or half-antibody.

41. The composition of claim 40, wherein the antibody is an IgG4 antibody.

42. The composition of claim 41, wherein the antibody is an anti-integrin antibody.